

MOUSE *Fkh^f* cDNA SEQUENCE

1 GCTGATCCCC CTCTAGCAGT CCACITTCACC AAGGTGAGCG AGTGTCCCTG
 51 CTCTCCCCCA CCAGACACAG CTCTGCTGGC GAAAGTGGCA GAGAGGTATT
 101 GAGGGTGGGT GTCAGGAGCC CACCAGTACA GCTGGAAACA CCCAGCCACT
 151 CCAGCTCCCG GCAACTTCTC CTGACTCTGC CTTCAGACGA GACTTGGAAAG
 201 ACAGTCACAT CTCAGCAGCT CCTCTGCCGT TATCCAGCCT GCCTCTGACA
 251 AGAACCCAAT GCCAACCCCT AGGCCAGCCA AGCCTATGGC TCCTTCCTTG
 301 GCCCTTGGCC CATCCCCAGG AGTCTTGCCA AGCTGGAAGA CTGCACCCAA
 351 GGGCTCAGAA CTTCTAGGGA CCAGGGGCTC TGGGGGACCC TTCCAAGGTC
 401 GGGACCTGCG AAGTGGGCC CACACCTCTT CTTCTTGAA CCCCTGCCA
 451 CCATCCCAGC TGCACTGCC TACAGTGCCT CTAGTCATGG TGGCACCGTC
 501 TGGGGCCCGA CTAGGTCCT CACCCCACCT ACAGGCCCTT CTCCAGGACA
 551 GACCACACTT CATGCATCAG CTCTCCACTG TGGATGCCA TGCCCAGACC
 601 CCTGTGCTCC AAGTGGTCC ACTGGACAAC CCAGCCATGA TCAGCCTCCC
 651 ACCACCTTCT GCTGCCACTG GGGTCTTCTC CCTCAAGGCC CGGCCTGGCC
 701 TGCCACCTGG GATCAATGTG GCCAGTCTGG AATGGGTGTC CAGGGAGCCA
 751 GCTCTACTCT GCACCTTCCC ACGCTGGGT ACACCCAGGA AAGACAGCAA
 801 CCTTTGGCT GCACCCAAG GATCCTACCC ACTGCTGGCA AATGGAGTCT
 851 GCAAGTGGCC TGGTTGTGAG AAGGTCTTCG AGGAGCCAGA AGAGTTCTC
 901 AAGCACTGCC AAGCAGATCA TCTCTGGAT GAGAAAGGCA AGGCCAGTG
 951 CCTCCCTCCAG AGAGAAGTGG TGCAGTCTCT GGAGCAGCAG CTGGAGCTGG
 1001 AAAAGGAGAA GCTGGGAGCT ATGCAGGCC ACCTGGCTGG GAAGATGGCG
 1051 CTGGCCAAGG CTCCATCTGT GGCCCTCAATG GACAGAGACT CTTGCTGCAT
 1101 CGTAGCCACC AGTAATCAGG GCAGTGTGCT CCCGGCTGG TCTGCTCCTC
 1151 GGGAGGCTCC AGACGGCGGC CTGTTTGAG TGCGGAGGCA CCTCTGGGG
 1201 AGCCATGGCA ATAGTTCTT CCCAGAGTTC TTCCACAACA TGGACTACTT
 1251 CAAGTACCAAC AATATGCCAC CCCCTTCAC CTATGCCACC CTTATCCGAT
 1301 GGGCCATCCT CGAAGCCCCG GAGAGGCAGA GGACACTCAA TGAAATCTAC
 1351 CATTGGTTA CTCGCATGTT CGCCTACTTC AGAAACCCACC CGGCCACCTG
 1401 GAAGAATGCC ATCCGCACA ACCTGAGCCT GCACAAGTGC TTTGTGCGAG
 1451 TGAGAGCGA GAAGGGAGCA GTGTGGACCG TAGATGAATT TGAGTTTCGC
 1501 AAGAAGAGGA GCCAACGCC CAACAAGTGC TCCAATCCCT GCCCTTGACC
 1551 TCAAAACCAA GAAAAGGTGG GCGGGGGAGG GGGCCAAAAC CATGAGACTG
 1601 AGGCTGTGGG GGCAAGGAGG CAAGTCCCTAC GTGTACCTAT GGAAACCGGG
 1651 CGATGATGTG CCTGCTATCA GGGCCTCTGC TCCCTATCTA GCTGCCCTCC
 1701 TAGATCATAT CATCTGCCCT ACAGCTGAGA GGGGTGCCAA TCCCAGCCTA
 1751 GCCCCTAGTT CCAACCTAGC CCCAAGATGA ACTTTCCAGT CAAAGAGCCC
 1801 TCACAACCAG CTATAACATAT CTGCCTTGGC CACTGCCAAG CAGAAAGATG
 1851 ACAGACACCA TCCTAATATT TACTCAACCC AAACCCCTAAA ACATGAAGAG
 1901 CCTGCCTTGG TACATTCGTG AACTTTCAAA GTTAGTCATG CAGTCACACA
 1951 TGACTGCAGT CCTACTGACT CACACCCAA AGCACTCACC CACAACATCT
 2001 GGAACCACGG GCACTATCAC ACATAGGTGT ATATACAGAC CCTTACACAG
 2051 CAACAGCACT GGAACCTTCA CAATTACATC CCCCCAAACC ACACAGGCAT
 2101 AACTGATCAT ACGCAGCCTC AAGCAATGCC CAAAATACAA GTCAGACACA
 2151 GCTTGTCAAGA

Figure 1

MOUSE Fkh^{sf} PROTEIN SEQUENCE

1 MPNPRPAKPM APSIALGPSP GVLPSWKTAP KGSELLGTRG SGGPFQGRDL
51 RSGAHTSSSL NPLPPSQLQL PTVPLVMVAP SGARLGPSPH LQALLQDRPH
101 FMHQLSTVDA HAQTPVLQVR PLDNPAMISL PPPSAATGVF SLKARPGLPP
151 GINVASLEWV SREPALLCTF PRSGTPRKDS NLLAAPQGSY PLLANGVCKW
201 PGCEKVPEEP EEFLKHCQAD HLLDEKGKAQ CLLQREVVQS LEQQLELEKE
251 KLGAMQAHLA GKMALAKAPS VASMDKSSCC IVATSTQGSV LPAWSAPREA
301 PDGGLFAVRR HLWGSHGNSS FPEFFHNMDY FKYHNMRPPF TYATLIRWAI
351 LEAPERQRTL NEIYHWFTRM FAYFRNHPAT WKNAIRHNLS LHKCFVRVES
401 EKGAVWTVDE FEFRKRSQR PNKCSNPCP*

Figure 2

HUMAN *FKH*^f cDNA Sequence

096973-202100
1 GCACACACTC ATCGAAAAAA ATTTGGATTA TTAGAAGAGA GAGGTCTGCG
51 GCTTCCACAC CGTACAGCGT GGTTTTCTT CTCGGTATAA AAGCAAAGTT
101 GTTTTTGATA CGTGACAGTT TCCCACAAGC CAGGCTGATC CTTTTCTGTC
151 AGTCCACTTC ACCAACGCTG CCCCTGGACA AGGACCCGAT GCCCAACCCC
201 AGGCCTGGCA AGCCCTCGGC CCCCTCCTTG GCCCTTGGCC CATCCCCAGG
251 AGCCTCGCCC AGCTGGAGGG CTGCACCCAA AGCCTCAGAC CTGCTGGGGG
301 CCCGGGGCCC AGGGGAAACC TTCCAGGGCC GAGATCTCG AGGCAGGGCC
351 CATGCCTCCT CTTCTCCTT GAACCCCATG CCACCATCGC AGCTGCAGCT
401 GCCCACACTG CCCCTAGTCA TGGTGGCACC CTCCGGGGCA CGGCTGGGCC
451 CTTGGCCCCA CTTACAGGCA CTCCCTCAGG ACAGGGCACA TTTCATGCAC
501 CAGCTCTCAA CGGTGGATGC CCACGCCCGG ACCCCTGTGC TGCAGGTGCA
551 CCCCCCTGGAG AGCCCAGCCA TGATCAGCCT CACACCACCC ACCACCGCCA
601 CTGGGGTCTT CTCCCTCAAG GCCCGGCCCTG GCCTCCCACC TGGGATCAAC
651 GTGGCCAGGC TGGAATGGGT GTCCAGGGAG CGGGCACTGC TCTGCACCTT
701 CCCAAATCCC AGTGCACCCA GGAAGGACAG CACCCCTTCG GCTGTGCC
751 AGAGCTCCTA CCCACTGCTG GCAAATGGTG TCTGCAAGTG GCCCGGATGT
801 GAGAAGGTCT TCGAAGAGCC AGAGGACTTC CTCAAGCACT GCCAGGCGGA
851 CCATCTTCTG GATGAGAAGG GCAGGGCACA ATGTCTCCTC CAGAGAGAGA
901 TGGTACAGTC TCTGGAGCAG CAGCTGGTGC TGGAGAAGGA GAAGCTGAGT
951 GCCATGCAGG CCCACCTGGC TGGAAAATG GCACTGACCA AGGCTTCATC
1001 TGTGGCATCA TCCGACAAGG GCTCCTGCTG CATCGTAGCT GCTGGCAGCC
1051 AAGGCCCTGT CGTCCAGCC TGGTCTGGCC CCCGGGAGGC CCCTGACAGC
1101 CTGTTTGCTG TCCGGAGGCA CCTGTGGGGT AGCCATGGAA ACAGCACATT
1151 CCCAGAGTTC CTCCACAACA TGGACTACTT CAAGTTCCAC AACATGCGAC
1201 CCCCTTTCAC CTACGCCACG CTACATCCGCT GGGCCATCCT GGAGGCTCC
1251 GAGAAGCAGC GGACACTCAA TGAGATCTAC CACTGGTCA CACGCATGTT
1301 TGCCTTCTTC AGAAACCATC CTGCCACCTG GAAGAACGCC ATCCGCCACA
1351 ACCTGAGTCT GCACAAGTGC TTTGTGCGGG TGGAGAGCGA GAAGGGGGCT
1401 GTGTGGACCC TGGATGAGCT GGAGTTCCGC AAGAAACGGA GCCAGAGGCC
1451 CAGCAGGTGT TCCAACCTA CACCTGGCCC CTGACCTCAA GATCAAGGAA
1501 AGGAGGATGG ACGAACAGGG GCAAACACTGG TGGGAGGCAG AGGTGGTGGG
1551 GGCAGGGATG ATAGGCCCTG GATGTGCCCA CAGGGACCAA GAAGTGAGGT
1601 TTCCACTGTC TTGCCTGCCA GGGCCCTGT TCCCCGCTG GCAGCCACCC
1651 CCTCCCCCAT CATATCCTTT GCCCCAAGGC TGCTCAGAGG GGGCCCGGTC
1701 CTGGCCCCAG CCCCCACCTC CGCCCCAGAC ACACCCCCCA GTCGAGCCCT
1751 GCAGCCAAAC AGAGCCTTCA CAACCAAGCCA CACAGAGCCT GCCTCAGCTG
1801 CTCGCACAGA TTACTTCAGG GCTGGAAAAG TCACACAGAC ACACAAAATG
1851 TCACAATCCT GTCCCTCAC

Figure 3

HUMAN FKH^s PROTEIN SEQUENCE

1 MPNPRPGKPS APSLALGPSP GASPSWRAAP KASDLLGARG PGGTFQGRDL
51 RGGAHASSSS LNPMPPSQLQ LPTLPLVMVA PSGARLGPLP HLQALLQDRP
101 HFMHQLSTVD AHARTPVLQV HPLESPAMIS LTPPTTATGV FSLKARPGLP
151 PGINVASLEW VSREPALLCT FPNPSAPRKD STLSAVPQSS YPLLANGVCK
201 WPGCEKVFFEE PEDFLKHCQA DHLLDEKGRA QCLLQREMVQ SLEQQLVLEK
251 EKLSAMQAHL AGKMALTAKAS SVASSDKGSC CIVAAGSQGP VVPAWSGPRE
301 APDSLFAVRR HLWGSHGNST SPEFLHNMDY FKFHNMRRPF TYATLIRWAI
351 LEAPEKQRTL NEIYHWFTRM FAFFRNHPAT WKNAIRHNLS LHKCFVRVES
401 EKGAVWTVDE LEFRKKRSQR PSRCSNPTPG P*

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Figure 4

Vector for generation of FKHsf Transgenic mice

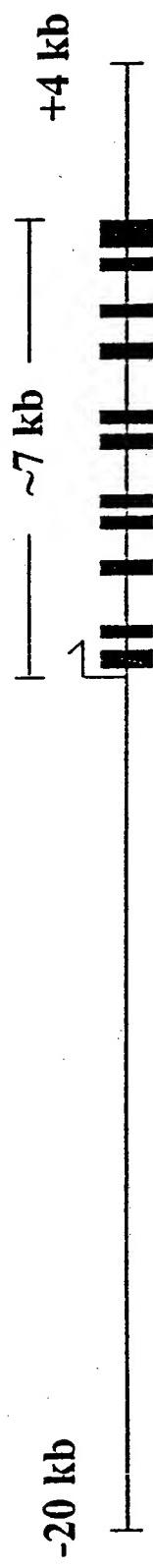


Figure 5

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FKHsf Transgene corrects the defect in scurvy animals

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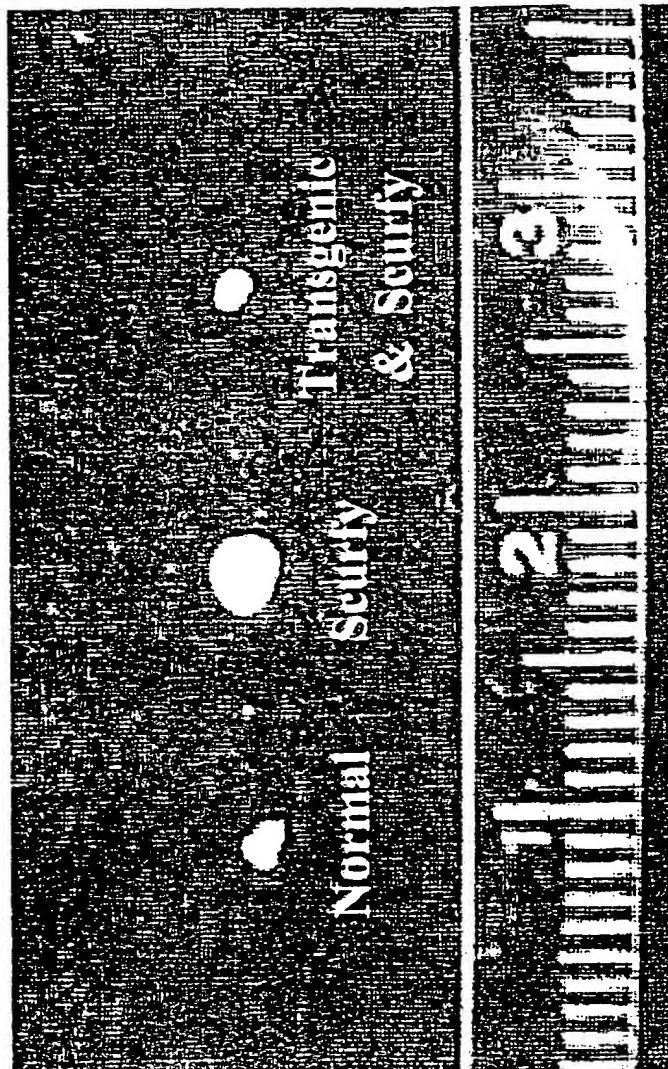


Figure 6

FKHsf tg mice have reduce lymph node cells
compared to normal cells

Cell number	Mouse genotype		
	Normal	Scurfy	Transgenic
Cells / LN	0.92	1.97	0.29
Cells / Thymus	0.76	0.54	0.76

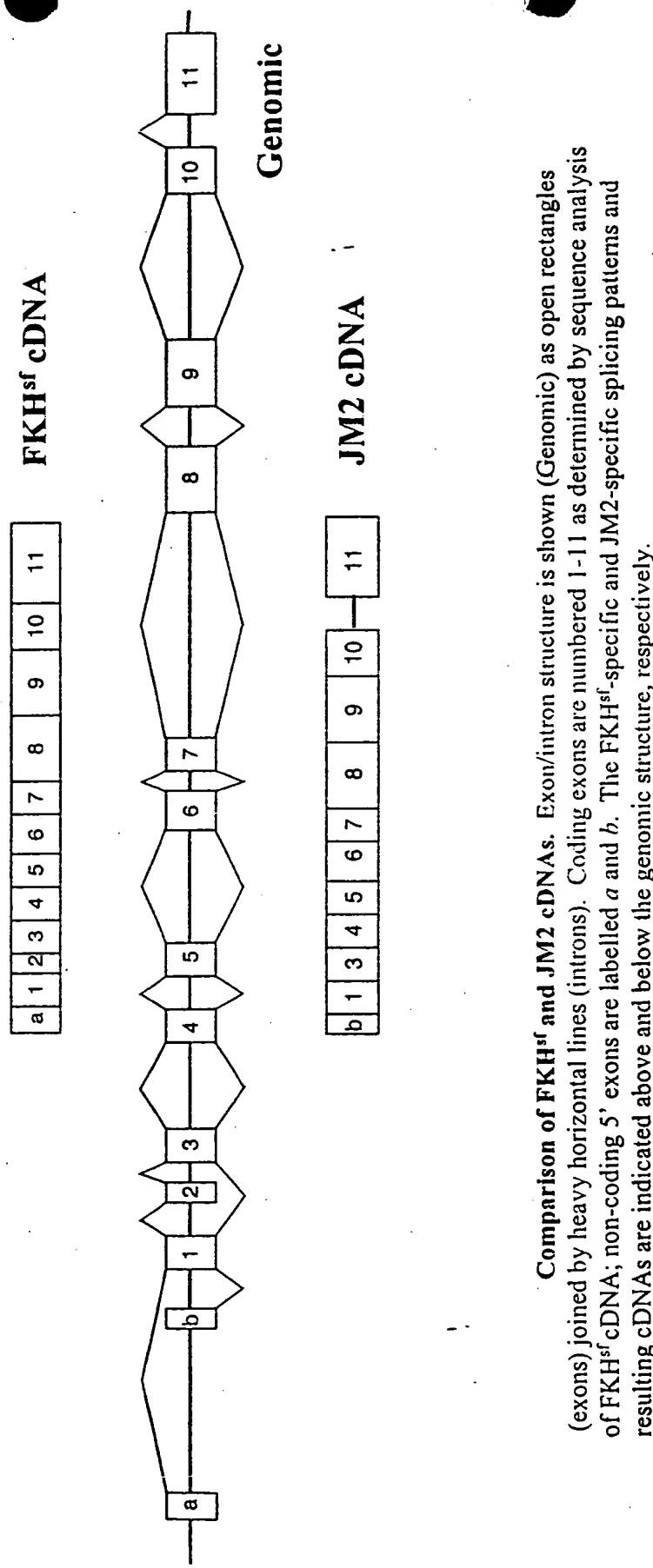
Figure 7

FKH_{sf} transgenic mice respond poorly to in vitro stimulation

Proliferation	Mouse genotype		
	Normal	Scurfy	Transgenic
No stimulation	778	23488	596
Anti-CD3+Anti-CD28	22932	225981	9106

Figure 8

Figure 9



Comparison of FKH^{sf} and JM2 cDNAs. Exon/intron structure is shown (Genomic) as open rectangles (exons) joined by heavy horizontal lines (introns). Coding exons are numbered 1-11 as determined by sequence analysis of FKH^{sf} cDNA; non-coding 5' exons are labelled *a* and *b*. The FKH^{sf}-specific and JM2-specific splicing patterns and resulting cDNAs are indicated above and below the genomic structure, respectively.

Human and mouse FK11sf proteins are highly conserved.

<i>N-terminal</i>	<i>ZNF</i>	<i>Mild</i>	<i>Forkhead</i>
83.4%	95.8%	82.8%	96.4%

Figure 10